General

Guideline Title

Non-small cell lung cancer stage IV.

Bibliographic Source(s)

Alberta Provincial Thoracic Tumour Team. Non-small cell lung cancer stage IV. Edmonton (Alberta): CancerControl Alberta; 2013 Nov. 23 p. (Clinical practice guideline; no. LU-004). [125 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Alberta Provincial Thoracic Tumour Team. Non-small cell lung cancer stage IV. Edmonton (Alberta): Alberta Health Services, Cancer Care; 2011 Jun. 16 p. (Clinical practice guideline; no. LU-004).

Recommendations

Major Recommendations

1. Whenever possible, patients with advanced non-small cell lung cancer (NSCLC) should be considered for eligibility in ongoing clinical trials.
2. Patients with a solitary metastasis as the basis for stage IV disease with good performance status and otherwise resectable and limited thoracic disease may benefit from more aggressive management, including surgical intervention and/or stereotactic radiotherapy.
3. Combination chemotherapy consisting of a platinum-based doublet is the standard of care for first-line treatment of advanced NSCLC (except for epidermal growth factor receptor [EGFR]-positive patients; see recommendation 6 below). The combination of three chemotherapeutic agents for the first-line treatment of advanced NSCLC is not routinely recommended based on current evidence.
4. Therapy should be continued for four cycles in most patients, and not more than six cycles in responding patients.
5. Acceptable alternatives to combination chemotherapy include non-platinum doublets or monotherapy:
    - For patients with a borderline performance status (PS=2), single-agent chemotherapy with vinorelbine, gemcitabine, paclitaxel, docetaxel or pemetrexed (for non-squamous cell carcinoma patients only) is recommended over best supportive care alone.
    - For elderly patients who cannot tolerate a platinum-based combination, single-agent chemotherapy with vinorelbine, gemcitabine, docetaxel, or pemetrexed (for non-squamous cell carcinoma patients only) is associated with improved survival and quality of life when compared to best supportive care alone. However, elderly patients with a good performance status (PS=0-1) should receive combination chemotherapy with a platinum-based doublet.
6. First-line monotherapy with the EGFR tyrosine kinase inhibitor gefitinib is recommended for patients with EGFR mutation-positive NSCLC.
7. Testing for EGFR mutations should take place for all eligible patients with advanced NSCLC and adenocarcinoma (including adenosquamous) histology who are being considered for first-line therapy with gefitinib, irrespective of their gender, ethnicity, and smoking

status.

8. Second-line or subsequent chemotherapy options for advanced NSCLC include single-agent docetaxel or erlotinib for patients with squamous cell carcinoma histology, or single agent treatment with a drug that has not been previously used.
9. Crizotinib has been approved for second-line treatment of patients who are positive for anaplastic lymphoma kinase (ALK)-rearrangements from the pan-Canadian Oncology Drug Review (pCODR) and has also been approved for provincial coverage in Alberta.
10. Testing for ALK mutations should take place for all eligible patients with advanced NSCLC and adenocarcinoma (including adenosquamous) histology who are being considered for second-line therapy with crizotinib.
11. Palliative radiotherapy is recommended for relief of specific symptoms and prophylactic prevention of symptom development.

Clinical Algorithm(s)

An algorithm titled "Treatment Algorithm" is provided in the original guideline document.

Scope

Disease/Condition(s)

Stage IV non-small cell lung cancer

Guideline Category

Management

Treatment

Clinical Specialty

Oncology

Pulmonary Medicine

Radiation Oncology

Thoracic Surgery

Intended Users

Advanced Practice Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To outline management decisions for patients with stage IV non-small cell lung cancer

Target Population

Adult patients over the age of 18 years with advanced non-small cell lung cancer

Interventions and Practices Considered

1. Consideration for eligibility in ongoing clinical trials
2. Surgical intervention
3. Stereotactic radiotherapy
4. Combination chemotherapy (platinum-based doublet; triple agent chemotherapy is not routinely recommended)
5. Alternatives to combination platinum-based chemotherapy: non-platinum doublets or single agent chemotherapy with vinorelbine, gemcitabine, paclitaxel, docetaxel, or pemetrexed (for non-squamous cell carcinoma only)
6. Testing for epidermal growth factor receptor (EGFR) mutations
7. EGFR tyrosine kinase inhibitor (gefitinib) for patients with EGFR mutation-positive non-small cell lung cancer
8. Testing for anaplastic lymphoma kinase (ALK) mutations
9. Crizotinib for second-line treatment of patients who are positive for ALK-rearrangements
10. Second-line chemotherapy (single-agent docetaxel or erlotinib or other drug not previously used)
11. Palliative radiotherapy
12. Best supportive care

Major Outcomes Considered

- Tumour response rate
- 1-year survival
- Time to progression
- Overall survival
- Adverse effects of therapy
- Quality of life

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Research Questions

Specific research questions to be addressed by the guideline document were formulated by the guideline lead(s) and Knowledge Management (KM) Specialist using the PICO question format (Patient or Population, Intervention, Comparisons, Outcomes).

Guideline Questions

- What is the recommended first-line therapy for patients with stage IV non-small cell lung cancer (NSCLC)?
- What is the role for epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors in first-line treatment of patients with stage IV NSCLC?
- What is the optimal second-line therapy for patients with stage IV NSCLC?
- What is the role of palliative radiotherapy in the management of patients with stage IV NSCLC?

Search Strategy

For the November 2013 guideline update, the treatment algorithm (see the original guideline document) was updated to reflect newly approved provincial coverage of both anaplastic lymphoma kinase (ALK) testing and crizotinib for second-line treatment of ALK-positive patients, to

describe how this new treatment fits in with overall care for lung cancer patients, and to reflect the specific indications (second-line therapy after a failed platinum doublet regimen).

For the January 2013 guideline update, the working group conducted a search for new or updated practice guidelines published since February 2011 by accessing the Web sites of the following organizations: Cancer Care Ontario, the British Columbia Cancer Agency, Cancer Care Nova Scotia, the National Comprehensive Cancer Network, the American Society of Clinical Oncology, the Scottish Intercollegiate Guidelines Network, the National Institute for Health and Clinical Excellence, and the European Society for Medical Oncology.

Medical journal articles were searched using the EMBASE (2011 to January 2013) and PubMed (February 2011 to January 2013) electronic databases; the references and bibliographies of articles identified through these searches were scanned for additional sources. The PubMed search terms were: treatment [MeSH heading] AND stage IV non-small cell lung cancer. The search was limited to the following publication types: humans, adult 19+ years, English, clinical trial, comparative study, controlled clinical trial, guideline, meta-analysis and practice guideline. This search strategy was modified as necessary and repeated in each of the other electronic databases. The working group excluded articles from the final review if they had a non-English abstract, were not available through the library system, or were published prior to 2011.

The working group reviewed the currency and acceptability of all relevant literature and updated published guidelines for the treatment for stage IV NSCLC.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Not stated

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Evidence was selected and reviewed by a working group comprised of members from the Alberta Provincial Thoracic Tumour Team and a Knowledge Management (KM) Specialist from the Guideline Utilization Resource Unit (GURU). A detailed description of the methodology followed during the guideline development process can be found in the Guideline Utilization Resource Unit Handbook (see the "Availability of Companion Documents" field).

Evidence Tables

Evidence tables containing the first author, year of publication, patient group/stage of disease, methodology, and main outcomes of interest are assembled using the studies identified in the literature search. Existing guidelines on the topic are assessed by the KM Specialist using portions of the Appraisal of Guidelines Research and Evaluation (AGREE) II instrument (http://www.agreetrust.org) and those meeting the minimum requirements are included in the evidence document. Due to limited resources, GURU does not regularly employ the use of multiple reviewers to rank the level of evidence; rather, the methodology portion of the evidence table contains the pertinent information required for the reader to judge for himself the quality of the studies.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Formulating Recommendations

The working group members formulated the guideline recommendations based on the evidence synthesized by the Knowledge Management (KM) Specialist during the planning process, blended with expert clinical interpretation of the evidence. As detailed in the Guideline Utilization Resource Unit Handbook (see the "Availability of Companion Documents" field), the working group members may decide to adopt the recommendations of another institution without any revisions, adapt the recommendations of another institution or institutions to better reflect local practices, or develop their own set of recommendations by adapting some, but not all, recommendations from different guidelines.

The degree to which a recommendation is based on expert opinion of the working group and/or the Provincial Tumour Team members is explicitly stated in the guideline recommendations. Similar to the American Society of Clinical Oncology (ASCO) methodology for formulating guideline recommendations, the Guideline Utilization Resource Unit does not use formal rating schemes for describing the strength of the recommendations, but rather describes, in conventional and explicit language, the type and quality of the research and existing guidelines that were taken into consideration when formulating the recommendations.

The working group reviewed the currency and acceptability of all relevant literature and updated published guidelines for the treatment for stage IV non-small cell lung cancer.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

The working group circulated a draft of the updated guideline to the entire provincial tumour team for final feedback and approval. This guideline was reviewed and endorsed by the Alberta Provincial Thoracic Tumour Team.

When the draft guideline document has been completed, revised, and reviewed by the Knowledge Management (KM) Specialist and the working group members, it is sent to all members of the Provincial Tumour Team for review and comment. This step ensures that those intended to use the guideline have the opportunity to review the document and identify potential difficulties for implementation before the guideline is finalized. Depending on the size of the document, and the number of people it is sent to for review, a deadline of one to two weeks will usually be given to submit any feedback. Ideally, this review will occur prior to the annual Provincial Tumour Team meeting, and a discussion of the proposed edits will take place at the meeting. The working group members will then make final revisions to the document based on the received feedback, as appropriate. Once the guideline is finalized, it will be officially endorsed by the Provincial Tumour Team Lead and the Executive Director of Provincial Tumour Programs.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate management of patients with stage IV non-small cell lung cancer

Potential Harms

Adverse events and toxicity associated with chemotherapy, including rash and diarrhea, and with radiation therapy, including radiation myelitis

Qualifying Statements

Qualifying Statements

The recommendations contained in this guideline are a consensus of the Alberta Provincial Thoracic Tumour Team and are a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

Implementation of the Guideline

Description of Implementation Strategy

- Present the guideline at the local and provincial tumour team meetings and weekly rounds.
- Post the guideline on the Alberta Health Services website.
- Send an electronic notification of the new guideline to all members of CancerControl Alberta.

Implementation Tools

Clinical Algorithm

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

End of Life Care

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2011 Jun (revised 2013 Nov)

Guideline Developer(s)

CancerControl Alberta - State/Local Government Agency [Non-U.S.]

Source(s) of Funding

CancerControl Alberta

There was no direct industry involvement in the development or dissemination of this guideline.

Guideline Committee

Alberta Provincial Thoracic Tumour Team

Composition of Group That Authored the Guideline

Members of the Alberta Provincial Thoracic Tumour Team include medical oncologists, radiation oncologists, surgical oncologists, nurses, pathologists, and pharmacists.

Financial Disclosures/Conflicts of Interest

Participation of members of the Alberta Provincial Thoracic Tumour Team in the development of this guideline has been voluntary and the authors have not been remunerated for their contributions. CancerControl Alberta recognizes that although industry support of research, education and other areas is necessary in order to advance patient care, such support may lead to potential conflicts of interest. Some members of the Alberta Provincial Thoracic Tumour Team are involved in research funded by industry or have other such potential conflicts of interest. However the developers of this guideline are satisfied it was developed in an unbiased manner.

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Alberta Provincial Thoracic Tumour Team. Non-small cell lung cancer stage IV. Edmonton (Alberta): Alberta Health Services, Cancer Care; 2011 Jun. 16 p. (Clinical practice guideline; no. LU-004).

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the Alberta Health Services Web site .

Availability of Companion Documents

The following is available:

- Guideline utilization resource unit handbook. Edmonton (Alberta): CancerControl Alberta; 2013 Jan. 5 p. Electronic copies: Available in Portable Document Format (PDF) from the Alberta Health Services Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on February 10, 2012. The information was verified by the guideline developer on March 30, 2012. This summary was updated by ECRI Institute on April 28, 2014. The updated information was verified by the guideline developer on May 23, 2014. This summary was updated by ECRI Institute on July 18, 2014 following the U.S. Food and Drug Administration advisory on Docetaxel.

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